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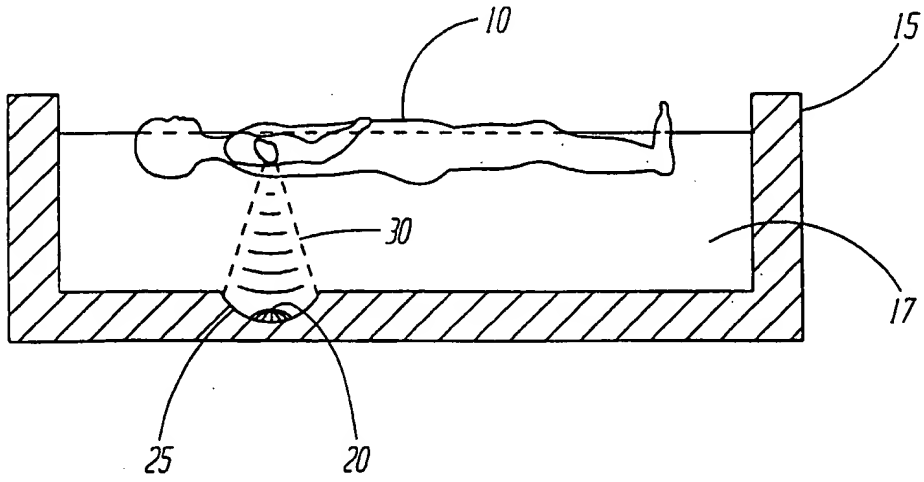
(54) Title: METHOD OF USING FOCUSED PRESSURE FRONTS IN MYOCARDIAL REVASCULARIZATION



(57) Abstract

A method of producing an angiogenic response in heart tissue using a lithotriptor.

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Method of Using Focused Pressure Fronts in Myocardial Revascularization

Field of the Invention

The present invention generally relates to cardiovascular disease. More specifically, the invention relates to myocardial revascularization. Those skilled in the art will recognize the benefits of applying the present invention to similar fields not discussed herein.

Background of the Invention

Extra-corporeal shock-wave lithotripsy (lithotripsy) is a medical procedure that has traditionally been used to disintegrate renal (kidney) stones. The term, lithotripsy is derived from a Greek work which literally means "stone crushing". This medical "stone crushing" technique has been demonstrated to be effective on kidney, upper ureteral and biliary stones (gallstones) in human patients. The technique is noninvasive and eliminates the need for the more conventional stone removal procedures, such as open surgery.

The number and variety of medical methods available to repair the effects of cardiovascular disease has increased rapidly over the last several years. More particularly, alternatives to open heart surgery and cardiovascular by-pass surgery have been extensively investigated, resulting in non-surgical procedures such as percutaneous transluminal coronary angioplasty, laser angioplasty, and atherectomy. These procedures are primarily directed toward the reduction of stenosis within the vasculature of a patient by either expanding the lumen through the use of a balloon, or ablating or otherwise removing the material making up the stenosis.

While these procedures have shown considerable promise, many patients still require bypass surgery due to such conditions as the presence of extremely diffuse stenotic lesions, the presence of total occlusions and the presence of stenotic lesions in

extremely tortuous vessels. Also, some patients are too sick to successfully undergo bypass surgery, and because the above treatments require surgical backup in the case of complications, they are untreatable. Some patients requiring repeat bypass surgeries are also untreatable.

One alternative to these procedures is known as Laser Myocardial Revascularization (LMR). In LMR, channels are formed in the heart wall with a laser. These channels provide blood flow to ischemic heart muscle. A history and description of this method is presented by Dr. M. Mirhoseini and M. Cayton in "Lasers in Cardiothoracic Surgery" in Lasers in General Surgery (Williams & Wilkins; 1989) pp. 216-223.

In the procedure described therein, a CO sub 2 laser is used to produce channels in the heart wall from the epicardium through the endocardium. This procedure follows a surgical cutdown. External pressure is used to stop bleeding from the interior of the heart to the outside. Dr. Mirhoseini has documented that although the channel is sealed at the epicardial layer, it remains patent in the endocardial and myocardial layers. Laser energy is transmitted from the laser to the epicardium by means of an articulated arm device that is commonly used for CO sub 2 laser surgery.

Further research in this general field indicated that the therapeutic benefits of the LMR procedure might not have been caused by increased perfusion but, instead, were an angiogenic affect stimulated by an injury to the heart wall. Typically, the heart does not re-grow muscle tissue which is dead. Angiogenises is the growth of vibrant muscle tissue in areas that have necrossed. Other methods of causing a heart wall injury include spark-ablation, mechanical injury, and direct injection of fluid. At a minimum, all know procedures currently are invasive or minimally invasive. Certainly, a non-invasive method of creating an angiogenic affect would be advantageous.

Summary of the Invention

The present invention improves upon the prior art by providing a non-invasive method of trans-myocardial revascularization. The invention further contemplates using commercially available lithotriptors to produce focused acoustic waves. The waves may be directed to heart tissue and thereby induce a controlled injury sufficient

to improve cardiac function. Control of the focus of the lithotriptor may provide the ability to create specific patterns of injury to the heart or to provide a diffuse injury over a relatively large portion of the heart wall.

Brief Description of the Drawings

Figure 1 depicts an electro-hydraulic lithotriptor.

Figure 2 depicts a diffuse injury pattern.

Figure 3 depicts an array of injuries.

Figure 4 depicts a stereotactic lithotriptor.

Detailed Description of the Invention

The following detailed description should be read with reference to the drawings in which like elements in different drawing are numbered identically. The drawings, which are not necessarily to scale, depict selected embodiments and are not intended to limit the scope of the invention.

Examples of constructions, materials, dimensions, and manufacturing processes are provided for selected elements. All other elements employ that which is known to those skilled in the field of the invention. Those skilled in the art will recognize that many of the examples provided have suitable alternatives that may also be used.

Lithotripsy requires a patient to be immersed in a large tank of water. Figure 1 depicts a patent 10 positioned in tank 15. Tank 15 is filled with water 17. Figure 1 further depicts a spark gap electrode 20 which generates shock waves 30. Shock waves 30 propagate through water 17 until shock waves 30 contact patient 10. The shock wave 30 may be directed to any part of the patient's body 10 through careful positioning of the patient 10 relative to the electrode 20 and by using a parabolic reflector 25 to focus the wave 30.

In general, the system depicted is an electro-hydraulic spark gap lithotriptor, which is commercially available from Dornier Medical Systems. Electro-hydraulic systems create a diverging pulse or explosion of energy which may be distributed over

an area of 15-20 square mm. Other systems include piezoelectric methods are available from Wolf. Inc. and electromagnetic methods from Siemens.

These other systems do not necessarily incorporate a tank of water. For example, piezoelectric systems create a focused shock wave by arranging a number of piezoelectric crystals in an array. That array may be affixed to the interior surface of a concave dish and thereby create focused waves. Advantageously, the converging wave of piezoelectric system may be focused on an area as small as 2-3 square mm. Furthermore, this system may be used with a patient who is positioned on a cushion or bag which is filled with water or an acoustic gel.

Any of the known lithotripsy systems available may, in the inventive method, be used to create an injury to cardiac tissue. As depicted in Figure 2, energy from the lithotriptor 35 may be diffusely focused on a relatively large portion 40 of the heart. Alternatively, Figure 3 depicts lithotriptor 35 intensely focused on the heart in such a way as to produce an array 45 of injured tissue.

Careful control of the lithotripsy system may be required to take full advantage. For instance, the system may be controlled by an ECG gating system to time the pulses with the patient's heart beats. Other acoustic or x-ray imaging systems could be used to control the focal point of the wave as the heart is moving.

Figure 4 depicts a stereotactic lithotripsy system which uses a number (3 shown) of spark gap wave generators 20 to direct and manipulate the pressure waves 30 from different angles for more precise control of the location of the injury to patient 10. An advantage of this system is that each of the generators 20 can be of lower energy but the focal points sees the same effective energy. This will result in precise focusing with little collateral damage to surrounding tissue.

It may be appreciated that drugs or genes may also be provided to augment the procedure and thereby improve any angiogenic affect. A wide variety of drugs or genes are known in the art including but not limited to thrombolytics, glycoproteins, anti-thrombotics, recombinant glycoproteins, anti-proliferatives, recombinant glycoproteins, antiarrhythmics, peptides, beta blockers, calcium channel blockers, recombinant peptide/proteins, vasodilators, recombinant peptide/proteins, genetic material, vasoconstrictors, inorganic ions or glycoproteins. Drugs may delivered locally, systemically or directly to a desired area of the heart. Drugs may be delivered before, after or during the lithotripsy procedure.

While the specification describes the preferred designs, materials, methods of manufacture and methods of use, those skilled in the art will appreciate the scope and spirit of the invention with reference to the appended claims.

We claim:

1. A method for producing a controlled injury response in heart tissue comprising:

focusing shockwave energy on the heart tissue.

2. The method of claim 1 further comprising:

providing a lithotriptor; and

controlling the lithotriptor such that the shockwave energy is focused on the cardiac tissue.

3. The method of claim 1 further comprising:

focusing the shockwave energy relatively diffusely about the cardiac tissue such that the energy is distributed over a relatively large amount of cardiac tissue.

4. The method of claim 1 further comprising:

focusing the shockwave energy on a relatively small amount of cardiac tissue.

5. The method of claim 4 further comprising:

focusing the shockwave energy on several different portions of the cardiac tissue such that an array of injuries is created.

6. The method of claim 2 further comprising:

providing controls which may time a pulse of shockwave energy with a beat of the heart.

7. The method of claim 2 further comprising:

providing a stereotactic lithotripsy system.

8. The method of claim 1 further comprising:

providing a drug or gene to the cardiac tissue before, after or during focusing of shockwave energy upon the cardiac tissue.

9. A method for inducing angiogenesis in a human heart comprising:

focusing a shock wave on the heart.

10. The method of claim 9 further comprising:

providing a lithotriptor as a source of the shock wave.

11. The method of claim 10 further comprising:

providing at least two lithotriptors aligned such that the shock waves produced by the lithotriptors impact the heart from different directions.

12. The method of claim 9 further comprising:

controlling the timing of the shock waves to coincide with the beating of the heart.

13. The method of claim 9 further comprising:

producing a diffuse injury to the heart.

14. The method of claim 9 further comprising:

producing an array of injured areas on the heart.

15. The method of claim 9 further comprising:

introducing a drug or gene into the heart.

16. A system for producing an angiogenic injury in a human heart comprising:

an array of lithotriptors focused on the heart.

17. The system of claim 16 further comprising controls which time pressure waves generated by the lithotriptor to coincide with beating of the heart.

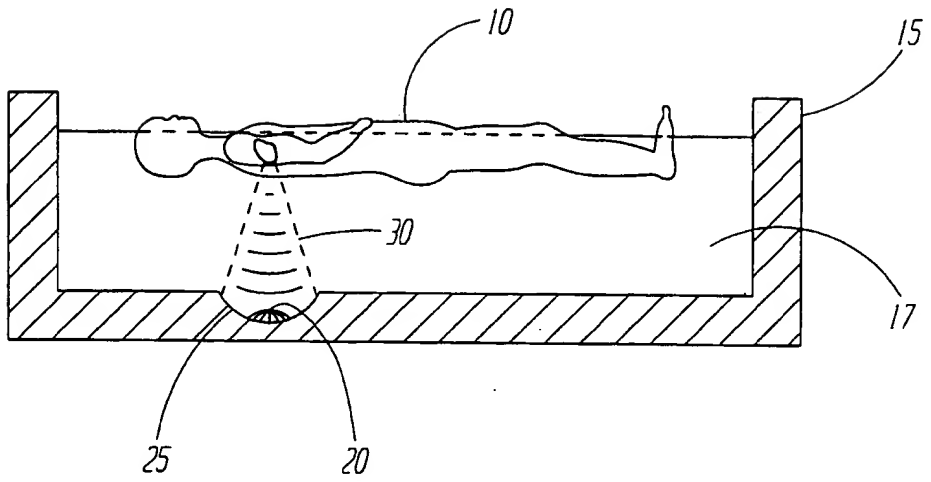

FIGURE 1

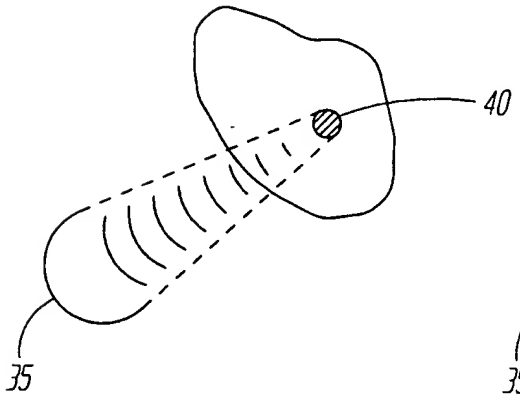

FIGURE 2

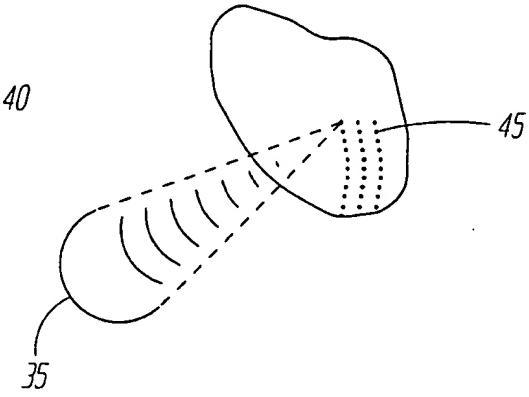

FIGURE 3

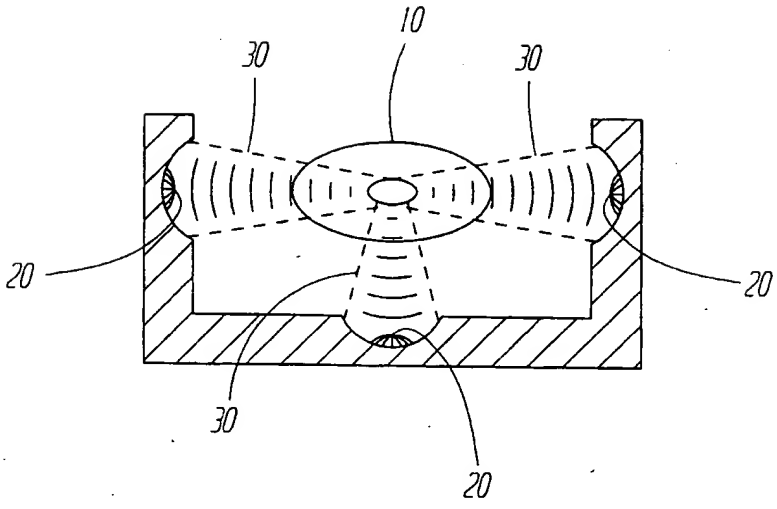

FIGURE 4

INTERNATIONAL SEARCH REPORT

Inte ional Application No
PCT/US 00/04484

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 A61B17/22 A61N7/00

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 A61B A61N

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 4 957 099 A (HASSLER DIETRICH) 18 September 1990 (1990-09-18) column 1, line 7 - line 13; figure 1	16
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Y	DE 195 43 741 C (WOLF GMBH RICHARD) 22 May 1997 (1997-05-22) column 1, line 1 - line 13; figure 1	16

-/—

[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

* Special categories of cited documents :

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Date of the actual completion of the international search	Date of mailing of the international search report
23 May 2000	06/06/2000

Name and mailing address of the ISA	Authorized officer
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PCT/US 00/04484

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	DE 38 12 838 A (SCHUBERT WERNER) 2 November 1989 (1989-11-02) the whole document	16
A	DE 43 12 264 A (SIEMENS AG) 20 October 1994 (1994-10-20) abstract; figure 1	16
A	US 4 693 247 A (BRISSON ALFRED G ET AL) 15 September 1987 (1987-09-15) abstract; figures 1-4	16,17

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INTERNATIONAL SEARCH REPORT

International application No.
PCT/US 00/04484

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

2. ☐ Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:

3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.

2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:

4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

☐ The additional search fees were accompanied by the applicant's protest.

☐ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

Information on patent family members

Inter nal Application No
PCT/US 00/04484

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